



General

Guideline Title

Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation.

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Mar. 44 p. (Technology appraisal guidance; no. 249).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Dabigatran etexilate is recommended as an option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with nonvalvular atrial fibrillation with one or more of the following risk factors:

- Previous stroke, transient ischaemic attack or systemic embolism
- Left ventricular ejection fraction below 40%
- Symptomatic heart failure of New York Heart Association (NYHA) class 2 or above
- Age 75 years or older
- Age 65 years or older with one of the following: diabetes mellitus, coronary artery disease or hypertension.

The decision about whether to start treatment with dabigatran etexilate should be made after an informed discussion between the clinician and the person about the risks and benefits of dabigatran etexilate compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to dabigatran etexilate should be considered in light of their level of international normalised ratio (INR) control.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Atrial fibrillation (AF)
- Stroke
- Systemic embolism (SE)

Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Risk Assessment

Treatment

Clinical Specialty

Cardiology

Geriatrics

Internal Medicine

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation

Target Population

Patients in England and Wales with atrial fibrillation and one or more of the following risk factors:

- Previous stroke, transient ischaemic attack or systemic embolism
- Left ventricular ejection fraction below 40%
- Symptomatic heart failure of New York Heart Association (NYHA) class 2 or above
- Age 75 years or older
- Age 65 years or older with one of the following: diabetes mellitus, coronary artery disease or hypertension

Interventions and Practices Considered

1. Dabigatran etexilate

Major Outcomes Considered

- Clinical effectiveness
 - Incidence of stroke or non-central nervous system embolism
 - Incidence of myocardial infarction
 - Vascular and all-cause mortality
 - Adverse events, including incidence of haemorrhage
 - Compliance/discontinuation of treatment
 - Health-related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Evidence Review Group (ERG) report for this technology appraisal was prepared by the Centre for Reviews and Dissemination (CRD), Centre for Health Economics (CHE), University of York (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of Methods Used by the Manufacturer to Systematically Review Clinical Effectiveness Evidence

The manufacturer's submission (MS) included two systematic reviews: the first of dabigatran trials in the relevant indication, and the second of all potentially relevant pharmacological interventions for the prevention of stroke in patients with atrial fibrillation (AF).

Manufacturer's Search Strategy

The manufacturer conducted extensive searches using a range of databases. For the first review of dabigatran trials in the relevant indication MEDLINE, EMBASE, CENTRAL, the manufacturer's own internal databases (BILIT, pre-BILIT and IDEA), Clinicaltrials.gov, and the proceedings of five relevant conferences were searched. Only English language studies were sought for this review, therefore language bias can't be ruled out.

For the second review of all potentially relevant pharmacological interventions for the prevention of stroke in patients with AF, MEDLINE, EMBASE, CENTRAL, Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), BIOSIS, and the reference lists of articles, reviews and meta-analyses were searched. No date or language restrictions were applied to the searches for the second review.

The search strategies used were reported in full for each section of the clinical review (clinical evidence, mixed treatment comparison [MTC], non-RCT evidence, adverse events) and seem appropriate; no relevant studies appear to have been missed.

Inclusion/Exclusion Criteria Used in the Study Selection

The inclusion and exclusion criteria applied in the MS to select studies for the first review of the efficacy and safety of dabigatran were:

Population: Adults (≥ 18 years) with AF

Intervention: Dabigatran

Comparator: Another treatment modality or placebo

Outcomes: Prevention of stroke

Study design: Randomised controlled trials or observational studies

The inclusion and exclusion criteria applied to select studies for the second review of other therapeutic regimens were:

Population: Adults (≥ 18 years) with AF

Intervention: Any treatment used to prevent stroke in AF

Comparator: Any alternative treatment used to prevent stroke in AF or placebo

Outcomes: Prevention of stroke

Study design: Randomised controlled trials

The inclusion criteria were applied by more than one reviewer in both reviews, reducing the potential for selection bias and missed studies.

Cost-effectiveness

Literature Search

The manufacturer carried out a comprehensive search of economic evaluation studies evaluating the cost-effectiveness of dabigatran etexilate in patients with AF. No previously published economic evaluations of dabigatran for preventing stroke in AF patients were identified by the manufacturer searches.

Electronic databases (EMBASE, MEDLINE, MEDLINE® In-process, National Health Service Economic Evaluation Database [NHS EED], EconLIT) were examined from 1990 up to the 5th July 2010. The search strategies used for each database are shown in the MS. In addition to the literature databases, conference proceedings from International Society on Pharmacoeconomics and Outcomes Research (ISPOR) Annual International Meeting 2008 and 2009, and ISPOR Annual European Congress 2008 and 2009 were hand searched. Table 65 of the MS summarises the eligibility criteria used to select possibly relevant studies. The literature search retrieved 1,251 studies. All of these studies were subsequently excluded.

Number of Source Documents

Clinical Effectiveness

Three randomised controlled trials (RCTs) that directly compared dabigatran with warfarin were included in the review.

Cost-effectiveness

- No published cost-effectiveness analyses were identified.
- The manufacturer submitted an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Evidence Review Group (ERG) report for this technology appraisal was prepared by the Centre for Reviews and Dissemination (CRD), Centre for Health Economics (CHE), University of York (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Data Extraction

Data were extracted in order to calculate hazard ratios (HR) or risk ratios (RR) with 95% confidence intervals (CI) by more than one reviewer, reducing the potential for data extraction errors.

Meta-analysis

Meta-analysis of the three trials comparing dabigatran to warfarin was not conducted for either the effectiveness or safety outcomes; PETRO and 1160.49 were short-term drug safety trials with no primary efficacy outcome and low incidence of safety outcomes, and the RE-LY was substantially larger than the other two trials. This decision seems appropriate.

Clinical Effectiveness Evidence Submitted

The manufacturer's submission (MS) included two generally well-conducted systematic reviews: the first of dabigatran trials in the relevant indication, and the second of all potentially relevant pharmacological interventions for the prevention of stroke in patients with atrial fibrillation (AF). The ERG found no relevant studies that were not discussed in the submission.

For the review of trials of dabigatran in the relevant indication the manufacturer identified three trials that directly compared dabigatran with warfarin: RE-LY, PETRO and 1160.49. The MS appropriately concentrated on the results of the RE-LY trial. The RE-LY trial was a good quality trial with blinded doses of dabigatran and an open-label dose warfarin arm. The other two trials were smaller phase II dose-finding studies with safety as the primary objective. The RE-LY trial was designed to demonstrate the non-inferiority of dabigatran compared to warfarin. This was appropriate given the well established efficacy of warfarin. Non-inferiority trials have limitations, particularly in relation to the establishment of the non-inferiority margin and the population on which to base analyses. However, the ERG feel that the manufacturer took adequate measures to reduce the impact of the potential biases associated with these limitations by using two margins of non-inferiority (1.46 and 1.38) and by analysing the results for both the intention to treat (ITT) and per protocol populations.

The software chosen to run the mixed treatment comparison (MTC) had some limitations: the inability to include trials with zero counts and the use of a fixed effect model that produced narrower confidence intervals which may not have reflected the heterogeneity across the trials. In addition, adjustment was made for only a single covariate in the analysis, and no justification as to the choice of that covariate over another that showed significant impact on the results of four major outcomes was given. The impact of the introduction of a fourth arm to the RE-LY trial into the MTC (and potentially double counting a large number of patients) on the relative effect of dabigatran, not only compared to dose-adjusted vitamin K antagonist (VKA), but also compared to aspirin monotherapy and aspirin plus clopidogrel, is uncertain. The importance of the MTC in the manufacturer's submission was limited: only the comparison with aspirin and aspirin plus clopidogrel were utilised in the economic model's base-case; the primary comparator in clinical practice for dabigatran is warfarin. It is worth noting that in the economic section of the submission, the manufacturer defines two 'dabigatran sequences' that fed into the model: neither of these were the dabigatran sequence arm that was created for the MTC.

See Section 4 of the ERG report (see the "Availability of Companion Documents" field) for more information on clinical effectiveness analysis.

Cost-effectiveness

Natural History

A Markov model was employed to follow AF patients through the natural course of the disease. The manufacturer chose a Markov model for three reasons: (1) it allows for the representation and transition between health states relevant to the condition; (2) it is an approach used in the economic evaluation literature for the modelling of AF; and (3) usability and accessibility of Markov models. A simplified model diagram is presented in Figure 3 of the ERG report (see the "Availability of Companion Documents" field).

There are 23 possible health states: 14 permanently active, 8 temporary states for patients who have discontinued therapy during one cycle due to extracranial haemorrhage (ECH), and the final state, death. Table 23 of the ERG report (see the "Availability of Companion Documents" field) describes how the events have been modelled to influence the transition of the patients between health states.

The model estimates costs and outcomes over the lifetime of the patient's cohort (up to 100 years). The outcomes considered are:

- The clinical events included in the model (ischaemic stroke, intracranial haemorrhage [ICH], haemorrhagic stroke, ECH, systemic embolism [SE], transient ischaemic attack [TIA], and acute myocardial infarction [MI])
- Quality of life (as quality-adjusted life years [QALYs])
- Life years accrued

All clinical outcomes are associated with acute costs and disutility. Further longer-term costs and disutility beyond the acute stage are only associated with ischaemic stroke, haemorrhagic stroke and ICH.

The Markov cycle length in the model is 3 months and only one event per cycle is permitted. The manufacturer provided three reasons for this decision. First, 3 months should reflect the typical duration of temporary drug discontinuation due to ECH. Second, the likelihood of patients experiencing more than one major event during 3 months is claimed to be low. Third, disability and mortality due to stroke are suggested to plateau at around 3 months.

Model Validation

According to the MS, the economic model was validated in three distinct levels:

- Revision and approval by key opinion leaders
- Validation of the mathematical relations and numerical inputs used by a modeller not involved in the construction of the model
- Substantiation of face validity

The ERG was unable to validate all aspects of the manufacturer's model. The results of the model were run using a visual basic macro. In calculating the results the model ran a Markov trace for each CHADS₂ score and by stroke history, but then cleared the results of each trace before calculating the next. This made it difficult to see how changes in the model affected different patient groups. It also made the model very slow to run. To calculate a single probabilistic sensitivity analysis (PSA) result required 10 hours computation time.

See Sections 5 and 6 of the ERG report (see the "Availability of Companion Documents" field) for more information on methods of cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a

document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The manufacturer's economic evaluation was based on a cost–utility analysis designed to compare the costs and outcomes of dabigatran with treatments used in the UK (warfarin, aspirin and aspirin plus clopidogrel). The manufacturer developed a Markov model that used three levels of disability (independent, moderate and severe) and death to define health states.

The manufacturer presented two economic models: a single-dose model and a sequential regimen model. In the single-dose model, the cohort with atrial fibrillation received either 110 mg twice daily or 150 mg twice daily throughout their treatment. In the sequential regimen model, the cohort was divided by age and modelled separately. The model for people younger than 80 years assumed that treatment began with dabigatran 150 mg twice daily, and switched to dabigatran 110 mg twice daily when the age of 80 years was reached. The model for people aged 80 years or older at baseline assumed a dose of dabigatran 110 mg twice daily throughout. Therefore, the sequential regimen model resulted in two sets of outputs: a sequential regimen model for people starting treatment younger than 80 years (incorporating a life-time horizon including the switch to 110 mg twice daily at 80 years) and a sequential regimen model for those starting treatment at 80 years or older.

The manufacturer reported pairwise cost-effectiveness results for dabigatran compared with warfarin. The incremental cost-effectiveness ratios (ICERs) for the dabigatran sequential regimen in which people started treatment when younger than 80 years and continued for the rest of their lives, and the sequential regimen in which people started treatment when older than 80 years were £7314 and £7873 per quality-adjusted life year (QALY) gained respectively, compared with warfarin. The ICERs for dabigatran 150 mg and 110 mg twice daily compared with warfarin were £6264 and £18,691 per QALY gained respectively.

The Evidence Review Group (ERG) commented that the RE-LY trial was of good quality and that the manufacturer appropriately concentrated on the results from this trial. The ERG highlighted the limitations of non-inferiority trials, such as establishing the non-inferiority margin and the population on which to base analyses. Overall, the ERG felt that adequate measures were taken by the manufacturer to reduce the impact of potential bias associated with non-inferiority trials.

The ERG carried out exploratory cost-effectiveness analyses by subgroups according to international normalised ratio (INR) control with warfarin. The ICER for dabigatran 150 mg twice daily compared with warfarin in people with perfect INR control (that is, in target INR range 100% of the time for the entire duration of treatment) was £60,895 per QALY gained. Dabigatran 110 mg twice daily was dominated by warfarin because it was associated with greater costs but lower health benefits. The group of people with poor INR control was also evaluated by the ERG. The ICER for dabigatran 150 mg twice daily compared with warfarin for people with an INR below 2 was £740 per QALY gained. For people with an INR above 3, warfarin was dominated by dabigatran 150 mg twice daily. The ERG did not include pairwise cost-effectiveness results for dabigatran in the sequential regimen compared with warfarin. The ERG concluded that INR control is a key parameter in the economic evaluation.

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Committee agreed with the ERG that the general approach taken by the manufacturer to estimate the lifetime cost-effectiveness of dabigatran was appropriate.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee concluded that the sequence of dabigatran 150 mg twice daily followed by dabigatran 110 mg twice daily once people reach 80 years would be the only regimen appropriate for the assessment of the cost-effectiveness of dabigatran relative to warfarin in the whole eligible UK population.

The Committee was aware that there was uncertainty around INR monitoring costs, which cohort most realistically reflected the population of people with atrial fibrillation in the UK, and whether disability and mortality were independent of the treatment received.

What Are the Key Drivers of Cost-effectiveness?

The Committee noted the ERG's comments that the cost-effectiveness of dabigatran compared with warfarin varied substantially according to level of INR control in those already being treated with warfarin.

Most Likely Cost-Effectiveness Estimate (Given as an ICER)

The Committee noted that the ERG's analysis, which included all of the requested assumptions, an INR monitoring cost, and the correct values for ischaemic stroke and disability rates increased the manufacturer's base-case ICER to £18,900 per QALY gained for the sequential regimen in people starting younger than 80 years, compared with warfarin. The Committee concluded that the most plausible ICERs for the whole population eligible for dabigatran were within the range normally considered a cost-effective use of National Health Service (NHS) resources, being less than £20,000 per QALY gained.

See Sections 3 and 4 of the original guideline document for details of the economic analysis provided by the manufacturer, the Evidence Review Group comments, and the Appraisal Committee considerations.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated for each recommendation.

The Appraisal Committee considered clinical and cost-effectiveness evidence and a review of this submission by the Evidence Review Group. For clinical effectiveness, three randomised controlled trials (RCTs) were the main source of evidence. For cost-effectiveness, the manufacturer's model was considered.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation

Potential Harms

The most common adverse events in people receiving dabigatran are anaemia, abdominal pain, diarrhoea, dyspepsia, gastrointestinal haemorrhage, genitourinary haemorrhage (patients may notice blood in their urine), nausea and nose bleeds.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Contraindications

Contraindications

- Dabigatran is contraindicated in people with severe renal impairment, active clinically significant bleeding, organic lesions at risk of bleeding, impairment of haemostasis, and hepatic impairment or liver disease expected to have an impact on survival.
- Concomitant treatment with systemic ketoconazole, cyclosporine, itraconazole or tacrolimus is also contraindicated.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE) and was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the National Health Service (NHS) in England and Wales on implementing National Institute for Health and Clinical Excellence (NICE) technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must usually provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. When there is no NICE technology appraisal guidance on a drug, treatment or other technology, decisions on funding should be made locally.
- NICE has developed tools to help organisations put this guidance into practice. These are available on the NICE Web site (<http://guidance.nice.org.uk/TA249>).

Implementation Tools

Audit Criteria/Indicators

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Mar. 44 p. (Technology appraisal guidance; no. 249).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Mar

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Dr Jane Adam (*Chair*), Department of Diagnostic Radiology, St George's Hospital; Professor Iain Squire (*Vice-Chair*) Consultant Physician, University Hospitals of Leicester; Professor A E Ades, Professor of Public Health Science, Department of Community Based Medicine, University of Bristol; Dr Jeremy Braybrooke, Consultant Medical Oncologist, University Hospitals Bristol NHS Foundation Trust; Dr Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool; Mr Christopher Earl, Surgical Care Practitioner, Renal Transplant Unit, Manchester Royal Infirmary; Mrs Eleanor Grey, Lay member; Professor Jonathan Grigg, Professor of Paediatric Respiratory and Environmental Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University London; Dr Peter Heywood, Consultant Neurologist, Frenchay Hospital; Dr Sharon Saint Lamont, Head of Quality and Innovation, North East Strategic Health Authority; Dr Ian Lewin, Consultant Endocrinologist, North Devon District Hospital; Dr Anne McCune, Consultant Hepatologist, University Hospitals Bristol NHS Foundation Trust; Dr Alec Miners, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine; Dr David Newsham, Lecturer (Orthoptics), University of Liverpool; Ms Pamela Rees, Lay member; Dr Ann Richardson, Lay member; Dr Paul Robinson, Medical Director, Merck Sharp & Dohme; Mr Stephen Sharp, Senior Statistician, MRC Epidemiology Unit; Mr Mike Spencer, Assistant Director Patient Experience, Cardiff and Vale University Health Board; Mr David Thomson, Lay member; Mr William Turner, Consultant Urologist, Addenbrooke's Hospital; Dr John Watkins, Clinical Senior Lecturer/Consultant in Public Health Medicine, Cardiff University and National Public Health Service Wales; Dr Anthony S Wierzbicki, Consultant in Metabolic Medicine/Chemical Pathology, Guy's and St Thomas' Hospitals NHS Trust; Dr Olivia Wu, Reader in Health Economics, University of Glasgow

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [National Institute of Health and Clinical Excellence \(NICE\) Web site](#) .

Availability of Companion Documents

The following are available:

- Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. Clinical audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012. 7 p. (Technology appraisal 249). Electronic copies: Available from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#) .
- Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. Electronic audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012. (Technology appraisal 249). Electronic copies: Available from the [NICE Web site](#) .
- Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation: evidence review group report. Centre for Reviews and Dissemination (CRD), Centre for Health Economics (CHE), University of York; 2011 Feb 4. 132 p. (Technology appraisal 249). Available in Portable Document Format (PDF) from the [NICE Web site](#) .

Patient Resources

The following is available:

- Dabigatran etexilate for preventing stroke and embolism in people with atrial fibrillation. Understanding NICE guidance. Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Mar. (Technology appraisal 249). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#) .

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NGC Status

This NGC summary was completed by ECRI Institute on July 3, 2012. This summary was updated by ECRI Institute on January 23, 2013 following the U.S. Food and Drug Administration advisory on Pradaxa (dabigatran etexilate mesylate).

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